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Glossary of Risk Assessment Related Terms (A - M)

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This glossary contains definitions of terms used frequently in IRIS. It is intended to users in understanding terms utilized by the U.S. EPA in hazard and dose-respons assessments. These definitions are not all-encompassing, but are useful "working definitions". It is assumed that the user has some familiarity with risk assessment a health science. For terms that are not included in this glossary, the user should refe standard health science, biostatistics and medical textbooks and dictionaries.

Acceptable Daily Intake (ADI): The amount of a chemical a person can be expos a daily basis over an extended period of time (usually a lifetime) without suffering deleterious effects.

Acute exposure: One dose or multiple doses of short duration spanning less than to 24 hours.

Acute toxicity: Any poisonous effect produced within a short period of time followi exposure, usually 24 to 96 hours.

Additional Risk (Added, Attributable Risk or Risk Difference) (AR): The calcula difference in risk of a particular condition between those who are exposed and thos are not. This measure is derived by subtracting the rate (usually incidence or morta the disease among the unexposed persons (Pu) from the corresponding rate amon exposed (Pe), i.e., AR= Pe-Pu. The AR is an absolute measure of the excess risk attributed to exposure.

Adverse Effect: A biochemical change, functional impairment, or pathologic lesion affects the performance of the whole organism, or reduces an organism's ability to to an additional environmental challenge.

Aerodynamic Diameter: The diameter of a sphere with unit density that has aerod behavior identical to that of the particle in question; an expression of aerodynamic b of an irregularly shaped particle in terms of the diameter of an idealized particle. Pa having the same aerodynamic diameter may have different dimensions and shapes

Aerosol: A suspension of liquid or solid particles in air.

Anecdotal Data: Data based on the description of individual cases rather than con studies.

Average Daily Dose (ADD): Dose rate averaged over a pathway-specific period of exposure expressed as a daily dose on a per-unit-body-weight basis. The ADD is u expressed in terms of mg/kg-day or other mass-time units.

Background Levels: Two types of background levels may exist for chemical subs

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Source: https://www.industrydocuments.ucsf.edu/docs/hxhj0001

(a) Naturally occurring levels: Ambient concentrations of substances present in the environment, without human influence; (b) Anthropogenic levels: Concentrations of substances present in the environment due to human-made, non-site sources (e.g. automobiles, industries).

Benchmark Dose (BMD) or Concentration (BMC): A statistical lower confidence the dose that produces a predetermined change in response rate of an adverse eff (called the benchmark response or BMR) compared to background.

Benchmark Response (BMR): An adverse effect, used to define a benchmark do which an RfD (or RfC) can be developed. The change in response rate over backgı the BMR is usually in the range of 5-10%, which is the limit of responses typically o in well-conducted animal experiments.

Benign tumor: A tumor that does not spread to a secondary localization, but may i normal biological function through obstruction or may progress to malignancy later.

Bioassay: An assay for determining the potency (or concentration) of a substance causes a biological change in experimental animals.

Bioavailability: The degree to which a substance becomes available to the target after administration or exposure.

Biologically Based Dose Response (BBDR) model: A predictive tool used to est potential human health risks by describing and quantifying the key steps in the cellu tissue and organismal responses as a result of chemical exposure.

Blood-to-air Partition Coefficient: A ratio of a chemical's concentration between l and air when at equilibrium.

Cancer: A disease of heritable, somatic mutations affecting cell growth and differer characterized by an abnormal, uncontrolled growth of cells.

Carcinogen: An agent capable of inducing cancer.

Carcinogenesis: The origin or production of a benign or malignant tumor. The carcinogenic event modifies the genome and/or other molecular control mechanisn target cells, giving rise to a population of altered cells.

Case-control study: An epidemiologic study contrasting those with the disease of (cases) to those without the disease (controls). The groups are then compared with to exposure history, to ascertain whether they differ in the proportion exposed to the chemical(s) under investigation.

Chronic Effect: An effect which occurs as a result of repeated or long term (chron exposures.

Chronic Exposure: Multiple exposures occurring over an extended period of time, significant fraction of the animal's or the individual's lifetime.

Chronic Study: A toxicity study designed to measure the (toxic) effects of chronic exposure to a chemical.

Chronic Toxicity: The capacity of a substance to cause adverse human health eff a result of chronic exposure.

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Source: https://www.industrydocuments.ucsf.edu/docs/hxhj0001

Co-carcinogen: An agent, when administered with a carcinogen, enhances the ac the carcinogen.

Cohort Study (or Prospective Study): An epidemiologic study comparing those w exposure of interest to those without the exposure. These two cohorts are then follc over time to determine the differences in the rates of disease between the exposur subjects.

Confounder (or Confounding Factor): A condition or variable that is both a risk f disease and associated with an exposure of interest. This association between the exposure of interest and the confounder (a true risk factor for disease) may make it appear that the exposure of interest is associated with disease.

Control Group (or Reference Group): A group used as the baseline for comparis epidemiologic studies or laboratory studies. This group is selected because it eithe the disease of interest (case-control group) or lacks the exposure of concern (coho study).

Critical Concentration: An ambient chemical concentration expressed in units of and used in the operational derivation of the inhalation RfC. This concentration will NOAEL Human Equivalent Concentration (HEC) adjusted from principal study data

Critical Effect: The first adverse effect, or its known precursor, that occurs to the r sensitive species as the dose rate of an agent increases.

Critical Study: The study that contributes most significantly to the qualitative and quantitative assessment of risk. Also called Principal Study.

Developmental Toxicity: Adverse effects on the developing organism that may re exposure prior to conception (either parent), during prenatal development, or postn until the time of sexual maturation. The major manifestations of developmental toxi include death of the developing organism, structural abnormality, altered growth, ar functional deficiency.

Dose-Response Assessment: A determination of the relationship between the ma of an administered, applied, or internal dose and a specific biological response. Re can be expressed as measured or observed incidence, percent response in groups subjects (or populations), or as the probability of occurrence within a population.

Dose-Response Relationship: The relationship between a quantified exposure (d and the proportion of subjects demonstrating specific, biological changes (respons

Effective Dose (ED10): The dose corresponding to a 10% increase in an adverse relative to the control response.

Endpoint: An observable or measurable biological event or chemical concentratior metabolite concentration in a target tissue) used as an index of an effect of a chem exposure.

Epidemiology: The study of disease patterns in human populations.

Estimated Exposure Dose (EED): The measured or calculated dose to which hur likely to be exposed considering all sources and routes of exposure.

Excess Lifetime Risk: The additional or extra risk of developing cancer due to exp

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Source: https://www.industrydocuments.ucsf.edu/docs/hxhj0001

a toxic substance incurred over the lifetime of an individual.

Exposure: Contact made between a chemical, physical, or biological agent and the boundary of an organism. Exposure is quantified as the amount of an agent availat exchange boundaries of the organism (e.g., skin, lungs, gut).

Exposure Assessment: An identification and evaluation of the human population to a toxic agent, describing its composition and size, as well as the type, magnitude frequency, route and duration of exposure.

Extra Risk (ER): A calculation of risk of adverse effects which adjusts for backgrou incidence rates of the same effects, by estimating risk at dose d only among the fra the population not expected to respond to the secondary (background) causes: ER P(0)/1-P(0)]. For example, if the background rate (P(0)) = 0.8 and the response rat dose d, P(d) = .9, then ER = (0.9 - 0.8)/(1-0.8) = 0.1/0.2 = 0.5. That is, at dose d, ar additional 10% of the population is expected to respond adversely. But since only 2 the population was expected to be free of adverse effects without the exposure of i this 10% represents 50% of the population that would otherwise have been unharm this exposure.

Extrapolation, low dose: An estimate of the response at a point below the range experimental data, generally through the use of a mathematical model.

Forced Expiratory Volume (FEV1): The volume of air that can be forcibly exhaled the first second of expiration following a maximal inspiration.

Forced Vital Capacity (FVC): The maximal volume of air that can be exhaled as f and rapidly as possible after a maximal inspiration.

Frank Effect Level (FEL): A level of exposure or dose which produces irreversible adverse effects at a statistically or biologically significant increase in frequency or s between those exposed and those not exposed.

Functional Residual Capacity (FRC): The lung volume at the end of tidal expirati - IC).

Gamma (Multi-hit) Model: A generalization of the one-hit model (see definition) fo dose extrapolation. The probability P(d) that an individual will respond to lifetime, continuous exposure to dose d is given by

$$P(d) = \{[a^{**}k]/G(k)\} \times \text{integral from 0 to d of } \{[t^{**}(k-1)]\exp(-at)\}dt$$

where G(k) = the gamma function,

k = the number of 'hits' estimated by the model, and

a = fitted coefficient.

Guidelines (human health risk assessment): Official, peer-reviewed documenta stating current U.S. EPA methodology in assessing risk of harm from environmenta pollutants to populations.

Examples:

Proposed Guidelines for Carcinogenic Risk Assessment: U.S.EPA guidelines inten guide Agency evaluation of suspect carcinogens. EPA/600/P-92/003C, April 1996.

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Source: https://www.industrydocuments.ucsf.edu/docs/hxhj0001

Guidelines for Exposure Assessment: U.S. EPA guidelines intended to guide Agen analysis of potential exposure to chemical substances. 51 FR 22888-22938; May 2

Guidelines for Developmental Toxicity Risk Assessment: U.S. EPA guidelines inter guide Agency analysis of developmental toxicity data. 51 FR 34028-34040, Octobe

Guidelines for the Health Risk Assessment of Chemical Mixtures: U.S. EPA guideli intended to guide Agency analysis of information relating to health effects from exp mixtures of chemical substances. 51 FR 34014-34025, September 1986.

Guidelines for Mutagenicity Risk Assessment: U. S. EPA guidelines intended to gui Agency analysis of mutagenicity data. 51 FR 34006-34016, September, 1986.

Hazard: A potential source of harm.

Hazard Assessment: The process of determining whether exposure to an agent c cause an increase in the incidence of a particular adverse health effect (e.g., cance defect) and whether the adverse health effect is likely to occur in humans.

Human Equivalent Concentration (HEC) or Dose (HED): The human concentrat inhalation exposure) or dose (for other routes of exposure) of an agent that is belie induce the same magnitude of toxic effect as the experimental animal species concentration or dose. This adjustment may incorporate toxicokinetic information o particular agent, if available, or use a default procedure, such as assuming that dai doses experienced for a lifetime are proportional to body weight raised to the 0.75 p

Incidence: The number of new cases of a disease that develop within a specified population over a specified period of time.

Incidence Rate: The ratio of new cases within a population to the total population a given a specified period of time.

Individual Risk: The probability that an individual will experience an adverse effec

Initiation: The first stage of carcinogenesis.

Interspecies Dose Conversion: The process of extrapolating from animal doses t human equivalent doses.

Latency Period: The time between first exposure to an agent and manifestation or detection of a health effect of interest.

Limited Evidence: A term used in evaluating study data for the classification of a carcinogen by the 1986 U.S. EPA guidelines for carcinogen risk assessment. This classification indicates that a causal interpretation is credible but that alternative explanations such as chance, bias, and confounding variables could not be comple excluded.

Linear dose response: A pattern of frequency or severity of biological response th proportionately with the amount of dose of an agent.

Linearized Multistage Procedure: A modification of the multistage model, used fo estimating carcinogenic risk, that incorporates a linear upper bound on extra risk fo exposures below the experimental range.

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Source: https://www.industrydocuments.ucsf.edu/docs/hxhj0001

Logistic Model: A dose-response model used for low-dose extrapolation, of the fo

$$P(d) = g + ([1 - g]/[1 + \exp(a + bd)])$$

where P(d) = probability of cancer from lifetime, continuous exposure at dose rate

a, b = fitted parameters; and

g = background incidence rate.

Lower limit on Effective Dose 10 (LED10): The 95% lower confidence limit of the a chemical needed to produce an adverse effect in 10 percent of those exposed to chemical, relative to control.

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at there are statistically or biologically significant increases in frequency or severity of effects between the exposed population and its appropriate control group. Also refe as lowest-effect level (LEL).

Lowest-Observed Effect Level (LOEL or LEL): In a study, the lowest dose or exp level at which a statistically or biologically significant effect is observed in the expos population compared with an appropriate unexposed control group.

Malignant Tumor: An abnormal growth of tissue which can invade adjacent or dist tissues.

Margin of Exposure (MOE): The LED10 or other point of departure divided by the or projected environmental exposure of interest.

Mass Median Aerodynamic Diameter (MMAD): Median of the distribution of airbo particle mass with respect to the aerodynamic diameter. MMADs are usually accon by the geometric standard deviation (g or sigma g) which characterizes the variabili particle size distribution.

Maximum Likelihood (ML) method, Maximum Likelihood Estimate (MLE): Stat method for estimating model parameters. Generally provides a mean or central ten estimate, as opposed to a confidence limit on the estimate.

Metastasis: The dissemination or secondary growth of a malignant tumor at a site from the primary tumor.

Model: A mathematical function with parameters that can be adjusted so the functi closely describes a set of empirical data. A mechanistic model usually reflects obse hypothesized biological or physical mechanisms, and has model parameters with re interpretation. In contrast, statistical or empirical models selected for particular num properties are fitted to data; model parameters may or may not have real world interpretation. When data quality is otherwise equivalent, extrapolation from mecha models (e.g., biologically based dose-response models) often carries higher confid than extrapolation using empirical models (e.g., logistic model).

Modifying Factor (MF): A factor used in the derivation of a reference dose or refe concentration. The magnitude of the MF reflects the scientific uncertainties of the s database not explicitly treated with standard uncertainty factors (e.g., the completei the overall database). A MF is greater than zero and less than or equal to 10, and t default value for the MF is 1.

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Source: https://www.industrydocuments.ucsf.edu/docs/hxhj0001

Monte Carlo Technique: A repeated random sampling from the distribution of valu each of the parameters in a calculation (e.g., lifetime average daily exposure), to de distribution of estimates (of exposures) in the population.

Multistage Model: A mathematical function used to extrapolate the probability of c from animal bioassay data, using the form

$$P(d) = 1 - \exp\{-[q(0) + q(1)d + q(2)d^{**}2 + \ldots + q(k)d^{**}k]\}$$

where: P(d) = probability of cancer from a continuous, lifetime exposure rate

q(i) = fitted dose coefficients of model; i = 0, 1, . . ., k; and

k = number of stages selected through best fit of the model, no greater than one le the number of available dose groups.

Multistage Weibull Model: A dose-response model for low-dose extrapolation wh includes a term for decreased survival time associated with tumor incidence:

$$P(d, t) = 1 - \exp\{-[q(0) + q(1)d + q(2)d^{**}2 + \ldots + q(k)d^{**}k]([t - t(0)]^{**}z)\}$$

where P(d,t)= the probability of a tumor (or other response) from lifetime, contin exposure at dose d until age t (when tumor is fatal);

qi = fitted dose parameters, i = 0, 1, . . ., k;

k = no greater than the number of dose groups - 1;

t(0) = the time between when a potentially fatal tumor becomes observable and v causes death (t(0) >= 1); and

z = fitted time parameter (also called "Weibull" parameter).

Mutagen: A substance that can induce an alteration in the structure of DNA.

N - ZGLOSSARY2

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Source: https://www.industrydocuments.ucsf.edu/docs/hxhj0001